

polynucleotide for which the coding sequence is as shown in SEQ ID NO:1.

8. (Amended) A polynucleotide according to claim 1 operably linked to a further polynucleotide comprising nucleic acid residues 5377 to 8527 of SEQ ID NO:1, corresponding to a 3' untranslated region, or a fragment thereof, or SEQ ID NO:1.

B1
9. (Amended) A recombinant DNA molecule in the form of an expression vector comprising an expression signal operably linked to a polynucleotide according to claim 1.

10. (Amended) A host organism transfected or transformed with the vector according to claim 9.

17. (Amended) Polypeptide according to claim 14 operably linked to the mature part of PAPP-A2 corresponding to amino acid residues 234 to 1791 of SEQ ID NO:2.

B2
18. (Amended) Polypeptide according to claim 12, wherein said polypeptide is a recombinant polypeptide.

19. (Amended) Polypeptide according to claim 12, wherein the polypeptide is free of human proteins, or other proteins natively associated with said polypeptide.

~~Claims 20 and 21 have been cancelled.~~

B3
22. (Amended) A method for producing an antibody with specificity for the polypeptide according to claim 12, said method comprising the steps of

i) providing a host organism,

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Cont
ii) immunizing the host organism with the polypeptide according to claim_12, and

iii) obtaining said antibody.

26. (Amended) A method for producing the polypeptide according to claim 18, said method comprising the steps of

i) providing a suitable host organism,

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ii) transfecting or transforming said host organism with an expression vector, said vector comprising an expression signal operably linked to a polynucleotide encoding said polypeptide,

iii) culturing the host organism obtained in step ii) under conditions suitable for expression of the polypeptide encoded by the polynucleotide or the vector; and optionally

isolating from the host organism the polypeptide resulting from recombinant expression by the host organism.

42. (Amended) A method of diagnosing a clinical condition in an individual, said method comprising the steps of

B5
i) performing the method of claim 30, and

ii) diagnosing the clinical condition.

B6
53. (Amended) An inhibitory agent obtainable according to the method of claim 49.

~~Claim 54 has been cancelled.~~

B⁷ 59. (Amended) An enhancing agent obtainable according to the method of claim 54.

~~Claim 60 and 61 have been cancelled.~~

65. (Amended) The method according to claim 63, wherein the clinical condition is selected from the group consisting of Down's syndrome, preeclampsia and acute coronary syndrome.

B⁸ 66. (Amended) The method according to claim 63, wherein the complex is PAPP-A/proMBP and the clinical condition is selected from the group consisting of Down's syndrome and acute coronary syndrome.

67. (Amended) The method according to claim 63, wherein the complex is proMBP/ANG and the clinical condition is Down's syndrome.

Claims 68 and 69 have been added:

68. (New) A method of treating a clinical condition mediated by IGFBP-5 which comprises administering to a subject in need thereof a therapeutically effective amount of the polypeptide of claim 12.

B⁹ 69. (New) A method of treating a clinical condition mediated by PAPP-A2 which comprises administering to a subject in need thereof a therapeutically effective amount of the inhibitory agent of claim 53.